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**Deficient Distracter Inhibition and Enhanced Facilitation for Emotional Stimuli in
Depression: An ERP Study**

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Abstract

The aim of the present study was to investigate distracter inhibition ability and facilitation for emotional faces in depression using a negative affective priming (NAP) task combined with event-related potentials (ERP). Participants were instructed to evaluate the valence of the target, which had been primed or inhibited on a preceding trial. The reaction times and the ERP amplitudes were recorded during the task. In a first behavioral experiment, control participants (NC), participants who were currently remitted (RMD), and participants diagnosed with a current major depressive disorder (MDD), performed a modified the NAP task. The main finding was that compared with NC groups, MDD participants had enhanced positive priming and less inhibition of sad faces. RMD individuals were characterized by general inhibitory impairments for all emotional faces and a facilitation for sad faces compared with NC individuals. In a second experiment combining the modified NAP task with ERP, the MDD participants had a larger P1 and P3 amplitude for sad faces in the positive priming condition compared with the other groups, and smaller P3 amplitude for sad faces in negative priming condition compared with other faces. Interestingly, RMD participants showed a distinct pattern of results compared with NC and MDD participants. They had larger N1 amplitude for happy faces and larger P1 and P3 amplitude for sad faces in the positive priming condition relative to the other conditions, while they had smaller P3 amplitude for both happy and sad faces in the negative priming condition. Across two experiments, it can be concluded that MDD participants have deficient distracter inhibition and excessive facilitation for negative stimuli. The RMD participants showed a mixed pattern of deficient distracter inhibition and excessive facilitation for both positive and negative stimuli, the results were largely consistent with our previous study. This deficiency has a high explanatory value for information-processing bias and the neuropsychological

impairments observed in depression.

Key words depression, attentional bias, distracter inhibition, negative priming task.

Deficient Distracter Inhibition for Emotional Stimuli in Depression: An ERP study

1 Introduction

Major depressive disorder (MDD) is a highly debilitating psychiatric disorder and is known for a high prevalence rate and marked risk of recurrence after remission (Goodwin et al., 2006; Taylor et al., 2009). The identification of vulnerability factors for the development, maintenance, and recurrence of MDD is an important challenge, crucial to the prevention and treatment of (recurrent) depression. From a cognitive perspective there is marked interest in delineating biases at the level of emotion processing. Traditionally, many of those information-processing studies have primarily focused on memory and attention. Recent findings indicate that depressed individuals display an attentional bias for negative material at more elaborative stages of information processing (Koster et al., 2005; De Raedt and Koster, 2010). Moreover, it was found that depressed individuals had a better memory for negative information (Matt et al., 1992; Walter et al., 2007; Taylor and John, 2004). At present, there is little explanation for the mechanisms underlying these information-processing characteristics in MDD.

In recent years there has been increasing research into the construct of inhibition in depression, which could provide an important link between memory, attention, and depression (Joormann et al., 2007). That is, the inability to inhibit processing of negative material may underlie attention and memory bias which can cause increased levels of negative affect. Two relevant aspects of inhibition can be of particular relevance to depression. First, inhibitory processes play an important role in reducing interference from (emotional) distracters. In this case emotional material is present at the *input level* of information processing. Second, inhibition is important in directing attention away from emotional material that has been processed but then needs to be removed from working memory in function of other goals. In the latter case inhibition of emotional material is a mental operation at the end-stage of processing. Empirical studies have showed that depression is

associated with impaired inhibition at both stages (Goeleven et al., 2006; Joormann, 2004; Joormann and Gotlib, 2008). In the present study we aimed to further investigate impaired inhibition of emotional material at the input level.

Research on inhibition of emotional material at the input level has typically used the Negative Affective Priming task (NAP). This task is an affective modification of the negative priming paradigm (Joormann, 2004). A complete trial in this task includes two separate trials: a prime trial and a probe trial. Note that the participants are not aware of this separation into prime and probe trials. These two types of trials involve a stimulus pair consisting of an affective distracter and a target (pictures of emotional faces) that are assigned, in this study, through the color of the faces (i.e., colored vs. black and white). The participant is instructed to evaluate the valence of the target (e.g. color picture), while ignoring (inhibiting) the distracter (e.g. picture in black and white). To investigate attentional inhibition, the correspondence between the valence of the distracter in the prime trial and the target in the probe trial is crucial. In the control condition, there is no similarity between prime distracter and probe target. However, in the negative priming condition both share the same valence. In this task, successful inhibition of the stimulus valence of the distracter in the prime trial slows down the response to the target in the probe trial when this target has the same valence as the distracter. In other words, responding to a negative face as probe target would be slower if the previous prime distracter was a negative face (experimental condition) compared to if the previous prime distracter was a positive face (control condition). This slowdown is referred to as the NAP effect and can be considered as a valid index of inhibitory function towards affective material (Wentura, 1999).

In a first study using the NAP task, Joormann (2004) showed that dysphoric individuals and remitted depressed patients (RMD) were characterized by impaired inhibition of negative words. Further study of this phenomenon in clinically depressed patients indicated that compared with never depressed (NC) and RMD,

MDD patients were characterized by impaired inhibition of negative material (Goeleven et al., 2006). Interestingly, there are mixed findings on the presence of impaired inhibition in RMD individuals with one study showing impaired inhibition of negative words (Joormann, 2004) but another study showing no impaired inhibition for sad facial expressions (Goeleven et al., 2006). Finally, it was found that induced negative mood did not impair inhibition of sad faces (Goeleven et al., 2007).

Moreover, there are at least two types of attention biases: attention disinhibition and attention facilitation. Research on healthy participants has often examined distraction inhibition effects (negative priming) as well as processing facilitation effects (positive priming) for stimuli simultaneously (Wright et al., 2006). However, the previous studies on depression using the NAP task only examined distracter inhibition (negative priming condition), showing reduced inhibition for negative information in MDD patients (e.g., Goeleven et al., 2006). Therefore, it is uncertain whether depressed individuals possess an enhanced facilitation as well as impaired inhibition for negative information. The absence of such positive priming trials could result in systematic deviations between specific valences in the prime and probe trial. Therefore, in the present study we also included a positive priming condition, in which the prime target had the same identity as the probe target (see Table 1 for an overview of all trial types). The effects of positive affective priming can be indexed by the degree to which responding to the probe target is faster by the previous prime target having the same valence. This allows examining the possibility of enhanced facilitation as well as impaired inhibition in a single design.

The behavioral findings in depression are complemented by recent neuroimaging data (Rogers et al., 2004). For instance, in event-related potentials (ERP) study, it was observed (Holmes and Pizzagalli, 2008) that MDD was associated with a pronounced error negativity effect (ACC signaling) but impaired connectivity between ACC and DLPFC, and abnormal posterior ERP amplitude (Zhu et al., 2010), causing reduced attentional control. Despite of these encouraging findings, neuropsychological studies on inhibition have typically used

the emotional Stroop task, which does not allow distinguishing between active selection of task relevant material and active inhibition of task-irrelevant (emotional) material (Hasher and Zacks, 1988). Moreover, it is noteworthy that no study has combined a negative and positive priming task to investigate neural alterations in depressed patients. Therefore, it would be important to combine the NAP task with ERP measures in depression research. The recording and analysis of ERPs is the preferred technique here as ERP allows to track, with a millisecond time-resolution, specific neural events related to inhibitory processes (Olofsson et al., 2008). With regard to the neural mechanisms, several specific components related to affective priming were examined in previous study, with the P1 component used as a marker of early, rapid processing of spatial stimuli; the N1 component reflected the attentional focus on target and a discrimination process within the focus of attention; P3 component reflected additional resources needed when the probe targets were still inhibited or updating of object-representations when objects were repeated (Kathmann et al., 2006; Taylor, 2002; Gibbons, 2006). In negative priming experiments, a smaller N1 amplitude was found. Since a repetition control condition elicited a similar N1 reduction, this was interpreted as a general adaptation effect with repetition (DeSchepper and Treisman, 1996). Ceballos et al. (2003) adopted a visual identity negative priming task and found larger P3 amplitudes and delayed P3 latencies. Similar effects with regard to P3 amplitude were observed in a recent study (Kathmann et al., 2006). It can be concluded that larger P3 amplitude in NAP task reflects the recruitment of attentional resources which are required for successful inhibition of emotional stimuli, while smaller P3 amplitude reflects deficient inhibition. Therefore, the specific components under investigation here are the P1 (time window 60–140 ms), N1 (100–200 ms), and P3 (200–450 ms).

The main aim of the present study was to examine the neural correlates associated with depression-related impaired inhibition over emotional material. To this end we included MDD patients and healthy controls. In order to examine whether this cognitive characteristic of depression disappears in remission we also included a

group of RMD patients (Atchley et al., 2007). In a first behavioral experiment we used the NAP task in an attempt to replicate and extend the findings of Goeleven et al. (2006) in order to depart from a reliable behavioral effect. In experiment 2 we combined the NAP task with ERP recordings. Our hypotheses were: ① in contrast to the NC participants, MDD individuals would show deficient distracter inhibition ability and enhanced facilitation for sad faces in the behavioral data in NAP task. ② In contrast to the NC participants, MDD individuals would show neurophysiological indices of deficient distracter inhibition ability and enhanced facilitation for sad faces on the N1, P1, and P3 components of the ERPs in NAP task. ③ There might be similarity and differentiation between MDD and RMD participants on the behavioral and ERP data in NAP task.

2 Experiment 1

2.1 Method

2.1.1 Participants

Three groups of participants took part in this study (Chinese-speaking adults between the ages of 18 and 40 years of age): NC, RMD, and MDD.

First, participants were surveyed by Beck Depression Inventory-II (BDI-II) and Beck Anxiety Inventory (BAI) (Liu and Shu, 1999). The Hamilton Depression Rating Scale (HDRS) (Liu and Shu, 1999) was also used to identify individuals who were likely to meet inclusion criteria of the three groups. The subjects were divided into 3 groups, using the Structured Clinical Interview (SCID; First et al., 1995) for the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, 4th ed.; American Psychiatric Association, 1994). The whole psychometric assessment including the experiment was completed within 1 week.

The BDI is a 21-item self-report inventory for measuring the severity of depressive symptoms (Beck et al., 1996; Chinese version: Liu and Shu, 1999). The BAI is a 21-item self-report inventory for anxiety symptoms

(Beck et al., 1988; Chinese version: Liu and Shu, 1999). The HRSD is a 24-item inventory for depressive symptoms administered by psychiatrists (Hamilton, 1960; Chinese version: Liu and Shu, 1999).

In total, the NC, RMD, and MDD groups were comprised of 17 participants, each. Inclusion criteria of NC participants were: scoring 4 or below on the BDI and BAI, no history of depressive disorder or any other mental disorders according to DSM-IV. Participants in this group were recruited through advertisement. Inclusion criteria of RMD participants were: (1) scoring 7 or below on the HDRS; (2) at least two depressive episodes in the past, with the latest onset at least 8 weeks ago. These participants were screened to determine whether they had fully recovered from depression according to the DSM-IV criteria. Participants in this group were recruited through contacting psychotherapists. Inclusion criteria of MDD participants were: (1) scoring 20 or higher on the HDRS and (2) being diagnosed by a psychiatrist according to the DSM-IV criteria for MDD (Liu and Shu, 1999). Ten MDD patients were out-patients. Seven of MDD participants were taking antidepressant medication (two were taking 20 mg or 30 mg paroxetine hydrochloride; three were taking 20 mg, 40 mg or 40 mg fluoxetine hydrochloride; two were taking 30 mg or 40 mg mirtazapine). Two RMD participants were taking antidepressant medication (one was taking 20 mg fluoxetine hydrochloride, the other 20 mg mirtazapine).

Participants were excluded for severe head trauma and learning disabilities, as well as current and lifetime psychotic symptoms, bipolar disorder, and alcohol or substance abuse within the past 6 months. All groups of participants had normal eyesight or corrected eyesight, no color blindness (tested using a seven color board), and were right-handed (as indicated on the Edinburgh Handedness Inventory; Oldfield, 1971). Groups were matched with respect to age and gender. There were more female participants in each group, reflecting the higher depression incidence in females.

2.1.2 Material

Two hundred and seventy emotional faces, developed by the psychological department of the Chinese academy of sciences, were used (Wang & Luo, 2005). All faces were adjusted to same size (about 260×300 pixels, approximately 9×10 cm). The predominant facial expression was judged by 17 psychological postgraduates. Faces which obtained the most unambiguous judgment from all judges (inter-rater reliabilities above .90), were further evaluated. Furthermore, faces were rated on valence (range: 1 [very unpleasant] to 7 [very pleasant]) and arousal (1 [calm] to 7 [excited]) by 70 undergraduates on a visual analog scale. Inclusion criteria of happy faces were: positive valence and moderate-high arousal value (valence > 5, arousal > 4); inclusion criteria of neutral faces, neutral valence (3 < valence < 5) and limited arousal value (arousal < 3); inclusion criteria of sad faces, negative valence (valence < 3) and moderate-high arousal value (arousal > 4). Sixty happy, neutral, and sad faces were obtained, respectively.

2.1.3 Procedure

The research protocol was approved by the local ethics committee. After a complete description of the research to the participants, written informed consent was obtained.

The E-prime package 1.2 (Psychological Software Tools, Inc. Sharpsburg, PA, USA) was used to control stimulus presentation and record response accuracy and latency. Participants sat 60 cm in front of the screen, they were required to keep their gaze on a central fixation cross and to keep the left forefinger on key “1” of the response box, keep the right forefinger on key “5”. Two faces appeared at the upper and lower half of the screen. One was black-and-white, the other was colored. Face size was 7.5×8.5 cm, they were 3 cm apart (measured from their edges). Participants were required to neglect the black-and-white faces (distracter) and had to evaluate the valence of the facial expressions of the colored faces (target) by pressing key “1” of the response box for happy faces and key “5” for sad faces. They were required to press as quickly and as accurately as possible. The emotional stimuli remained on the screen until the participants made a response.

The stimulus onset asynchronies (SOA) between prime and probe was 1400 ms plus reaction times, the inter trial interval (ITI) was 2000 ms (Goeleven et al., 2006). Participants completed 12 practice trials (with the experimenter present). After the practice phase, they completed the test trials (completed by participants alone, with the experimenter absent but available outdoor). The spatial positions of the target and distracter were matched; the presentation order of different conditions was randomized.

One trial consisted of emotional faces from the same actor. The test phase consisted of 180 trials, 60 trials for each condition (positive priming, negative priming, and control condition). In order to prevent participants developing a response set, the stimuli exposure duration of 15 trials included in these 180 trials were adjusted to 400ms (which meant that the faces in both prime and probe trials were presented almost not allowing any responding) (Liu et al., 2007), for other 15 trials in control condition, probe targets shared the same valence with prime targets and distracters. See table 1 and figure 1 for an overview.

2.1.4 Data-analytic strategy

The characteristics of the participants were analyzed by χ^2 analysis and a single factor ANOVA. The main analyses were conducted on the response latencies (ms) observed in the probe trial as dependent variable. As independent variables we included group (NC, RMD, MDD), valence (happy and sad faces) and trial type (positive priming, negative priming, and control condition) in a mixed-design analysis of variance (ANOVA). Subsequently separate analyses were performed for positive and negative priming ($p < .05$ as significant level, and post hoc tests were two-tailed).

2.2 Results

2.2.1 Group characteristics

There were no significant differences between the groups on the male/female ratio, $\chi^2=0.47$, $df=2$, $N=51$, $p=.79$, age, $F(2,48) < 1$, ns. There were significant differences between every two groups on the BDI,

$F(2,48)=293.40, p < .001$, BAI, $F(2,48)=388.49, p < .001$, and HDRS scores, $F(2,48)=616.10, p < .001$, with higher scores in the MDD group than in the NC and RMD groups. See table 2 for an overview.

2.2.2 Overall effects

Erroneous responses and outlying response times (below 300ms and above 2000ms) were removed from the analyses (0.75% and 1.24% respectively). Note that trials were only included in the reaction time analysis if a correct response was made in both prime and probe trial (Goeleven et al., 2006).

The mean reaction times are presented in Table 3. The overall ANOVA revealed a main effect of Group, $F(2,48) = 6.19, p = .004$, with slower responding in MDD individuals ($M = 944$ ms) and RMD ($M = 896$ ms) individuals compared with NC individuals ($M = 826$ ms). The interaction effects are of crucial importance to our hypotheses. There was a three-way interaction between trial type, valence, and group, $F(4,96) = 5.21, p < .001$. For better understanding of the three-way interaction we further examined the negative and positive priming condition separately.

2.2.3 Negative Priming

To investigate negative affective priming we calculated a NAP score by subtracting the mean RT on the control trials from the mean RT on the negative priming trials, for each valence. Higher scores on the NAP score reflect good inhibitory control. These NAP scores are depicted as a function of valence and group in Table 4. These NAP scores were then used as dependent variable in an ANOVA including valence and group as factors. This analysis showed a main effect of group, $F(2, 48) = 14.14, p < .001$, with overall larger NAP scores in the NC participants ($M = 62$ ms) than in the MDD ($M = -46$ ms) and RMD ($M = -42$ ms) participants. Importantly, there was a significant two-way interaction between valence and group, $F(2, 48) = 5.38, p = .007$. A univariate ANOVA showed that compared with RMD and MDD participants, NC individuals had a significant higher NAP score for sad faces, $F(2, 48) = 13.348, p < .001$. Interestingly, compared with NC

individuals, there was a significantly lower NAP score for happy faces in the RMD group, $F(2, 48)=4.57$, $p=.015$, but not in the MDD group, $F(2,48) <1$, ns. The NAP score for sad faces was not different between RMD and MDD individuals, $F(2,48) <1$, ns. Paired-samples t -tests within each group showed that only in the MDD individuals there was a significant difference between negative priming of sad versus happy faces, $t(16) = 2.84$, $p = .012$.

2.2.4 Positive Priming

To investigate positive affective priming we calculated a facilitation index by subtracting the mean RT on the control trials from the mean RT on the positive priming trials, for each valence. Lower scores on this index reflect enhanced priming by emotional information. These scores are also depicted as a function of valence and group in Table 4. The facilitation index was then used as dependent variable in an ANOVA including valence and group as factors. This analysis showed a main effect of group, $F(2, 48) = 10.48$, $p < .001$, with overall largest facilitation in the MDD participants ($M = -335$ ms), compared with the RMD ($M = -269$ ms) and the NC participants ($M = -181$ ms). There was a marginally significant two-way interaction between valence and group, $F(2,48) = 2.81$, $p = .07$. A univariate ANOVA showed that compared with RMD and MDD participants, NC individuals had significant higher facilitation for sad faces, $F(2, 48) = 11.69$, $p < .001$, but not for happy faces, $F(2, 48) = 2.11$, $p = .13$. The facilitation score for sad and happy faces were not significantly different between RMD and MDD individuals, $F(2,48) <1$, ns. Paired-samples t -tests within each group showed that only in the MDD individuals there was a significant difference between facilitation of sad versus happy faces, $t(16) = 2.46$, $p = .026$.

2.3 Discussion

Experiment 1 aimed to investigate positive and negative affective priming in MDD, RMD versus NC individuals. The outcomes were as follows: Compared with NC, MDD is characterized by reduced inhibition

and enhanced priming of sad but not happy material. RMD individuals were characterized by general inhibitory impairments for all emotional faces compared with NC individuals. These individuals showed a specific facilitation for sad faces. These main findings were confirmed when excluding medicated participants (MDD group, $n = 7$; RMD group, $n = 2$) since several patients were medicated (see Appendix A).

In previous study, we found that sub-clinically depressed individuals had deficient distracter inhibition for negative stimuli (Dai and Feng, 2007). However, the present study broadened the results by including RMD and MDD patients as participants. The deficient inhibition of negative information in MDD is in line with previous studies (Goeleven et al., 2006). Moreover, the present study is among the first to show that RMD is associated with distracter inhibitory deficits. These results are largely consistent with previous studies which found that RMD participants had deficient inhibition for negative material (Dai and Feng, 2009; Joormann, 2004). This may indicate that there is a cognitive “scar” of previous depressive episodes. Provided that there is no control condition with neutral material it is unclear whether RMD is associated with emotion-specific inhibitory deficits or whether this generalizes to non-emotional material as well (Frings and Wentura, 2008).

There are several noteworthy aspects of the positive priming data. There is some research indicating that affective priming effects are more pronounced in depression (Dannowski et al., 2006). Here it was observed that in MDD this enhanced priming effect is observed for sad faces. The divergence between patterns of valence specific effects in positive versus negative priming suggest that negative affective priming effects cannot be explained solely in terms of initial activation of emotional information. Instead, these data suggests that there are difficulties in depression in inhibiting sad faces.

A more extensive discussion of the behavioral findings is presented in the General Discussion. For now, Experiment 1 shows that depression is associated with replicable deficient inhibition of sad faces. In Experiment 2, the neural processes underlying this deficiency are examined using ERP.

3 Experiment 2

In Experiment 2 we used ERP recording to study cognitive inhibition of emotional faces in depression.

3.1 Method

Selection of participants, materials and procedure of experiment were similar to Experiment 1. 20 NC, 18 RMD and 19 MDD new participants were recruited. The test phase consisted of 180 trials, 60 trials for each condition.

The experimental apparatus (BrainAmp MR ERP system) was produced by the Brain Product GmbH; a 64 electrode Ag/AgCL Brain Amp MR Cap (Shenzhen Hanix United, Inc.) and an expanded 10-20 system were adopted. During recording, all channels were referenced to the frontal-central midline electrode (FCz). Brain electroencephalogram (EEG) activity (bandpass 0.01–30 Hz), horizontal and vertical electrooculograms (HEOG and VEOG) were tracked during the cognitive task. Two electrodes located medially to the right eye, one above and one below, were used to monitor vertical eye movements. Electrodes placed at the outer canthi of the eyes measured horizontal eye movements. Impedances for all the electrodes were kept below 3 k Ω . Signals were digitized by an AC-coupled amplifier at a sampling rate of 500 Hz. For ERP analysis, data were processed as follows: first, the ERPs were re-referenced to an average reference. Second, ERPs were extracted during the probe display from –200 to 1000 ms around the stimulus onset. Third, ocular artifacts were subtracted by a regression technique (Gratton et al., 1983). Afterwards, data were baseline-corrected with respect to the 200 ms pre-stimulus interval and digitally bandpass-filtered at 0.2–20 Hz (slope 24 dB). Finally, trials still containing artifacts in any EEG channel (maximum amplitude in the recording epoch ± 200 μ V; maximum difference between 2 successive sampling points 50 μ V; maximum difference of 2 values in the epoch 200 μ V; lowest allowed activity change 0.5 μ V in successive intervals of 100 ms) were excluded from averaging. The participants were asked to refrain from moving their heads.

The ERPs (at F3,Fz,F4,C3,Cz,C4,P3,Pz,P4,O1,Oz and O2 electrode) (Pérez-Edgar and Fox, 2003; Pérez-Edgar et al., 2006; van Hooff et al., 2008) were extracted by vision analyzer during the cognitive task from -200 to 1500 ms around stimulus onset of the faces on probe trials.

A mixed-design ANOVA with the same factors as in Experiment 1 was conducted to examine the behavioral data. A five-way 3 (group) \times 3 (trial type) \times 2 (valence) \times 2 (hemisphere: left and right) \times 4 (region: frontal, central, parietal and occipital) mixed-design ANOVA was conducted on the amplitudes and peak latencies of ERP (Shu, 2005). Greenhouse-Geisser corrections were applied when appropriate. Grand mean averages were calculated and the window of measurement for subsequent individual peak detection was determined by visual inspection of the grand means. Statistical analyses were performed on the mean voltages at various intervals of interest in the ERP waveform similar to those identified previously (van Hooff et al., 2008; Pérez-Edgar and Fox, 2003): P1, N1, and P3. The minimal 20 segments per condition were considered necessary for inclusion into the Grand Average (van Hooff et al., 2008; Doalloa et al., 2004), 17 participants of each group satisfied this threshold.

3.2 Results

The behavioral outcomes were highly similar to those of experiment 1, see Appendix B, Table B1 and B2 for details (Please note that, for length considerations, the behavioural data of exp. 2 was presented as supplementary material).

3.2.1 Group characteristics

There were no significant differences with respect to male/female ratio ($\chi^2=0.47$, $df=2$, $N=51$, $p=.790$), and age ($F < 1$, ns) among the three groups. By design, there were significant differences between the groups on the BDI, $F(2,48) = 195.69$, $p < .001$, BAI, $F(2,48)=355.86$, $p < .001$, and HDRS scores, $F(2,48)=640.45$, $p < .001$. See table 5 for an overview of participant characteristics.

3.2.2 ERP amplitude (Fig. 3 – Fig. 5)

(1) N1

An interaction effect was found between group, valence, trial type, and hemisphere, $F(4,96)=5.07, p=.001$.

To interpret the four-way interaction we examined amplitudes for different regions (frontal, central, parietal and occipital) separately. A significant interaction effect between group, valence, trial type, and hemisphere, was found only at the occipital site, $F(4,96)=3.62, p=.009$.

We further examined this interaction on the amplitudes of different hemispheres (left and right) separately.

A significant interaction effect was found between group, valence and trial type only at O2 electrode, $F(4,96)=2.47, p=.049$. A further 3×2 mixed ANOVA analysis was performed for the positive, control, and negative priming condition separately. None of the between group comparisons reached significance ($F_s < 1$). Moreover, a 2×3 repeated-measures ANOVA analysis was performed for NC, RMD and MDD participants, separately. Only in the RMD participants there was a significant interaction effect between valence and trial type, $F(2,32)=3.92, p=.03$. A univariate ANOVA revealed that RMD participants had a larger amplitude for happy faces in the control condition than in the other conditions, $F(2,48)=3.67, p=.033$. They had a larger amplitude for happy faces than for sad faces in the positive priming condition, $F(1,32)=6.74, p=.014$. None of the other group comparisons showed significant differences for the N1.

P1

A main effect was found for group, $F(2,48)=4.34, p=.018$, with an overall larger P1 amplitude for MDD participants compared with NC and RMD participants. The analysis also revealed an interaction effect between group, valence, trial type, hemisphere, and region, $F(12,288)=4.17, p<.001$. To further understand the five-way interaction we examined amplitudes for different regions (frontal, central, parietal and occipital) separately. This analysis showed an interaction effect between group, valence, trial type, and hemisphere only

at the occipital site, $F(4,96)=3.74, p=.007$.

A further ANOVA was conducted on the amplitudes of different hemispheres (left and right) separately. This analysis revealed an interaction effect between group and trial type only at the O2 electrode, $F(4,96)=5.48, p=.001$. Post hoc multiple comparisons revealed that there were significant differences in the amplitude for sad faces in the positive priming condition among the three groups, $F(2,48)=5.80, p=.006$. Specifically, the amplitude of MDD participants was larger compared with the other two groups. A further 2×3 repeated-measures ANOVA analysis was performed for NC, RMD and MDD participants separately in order to examine the within-subjects effects. There was a marginally significant interaction effect between valence and trial type in the MDD participants, $F(2,32)=3.26, p=.051$. A univariate ANOVA showed that MDD participants had a larger amplitude for sad faces compared with happy faces in the positive priming condition, $F(1,32)=4.68, p=.038$. They had a larger amplitude for sad faces in the positive priming condition compared with other conditions, $F(2,48)=4.11, p=.022$. Another univariate ANOVA revealed that RMD participants had a larger amplitude for sad faces in the positive priming condition compared with the other conditions, $F(2,48)=3.55, p=.036$. None of the other group comparisons showed significant differences for the P1.

P3

An interaction effect was found between group, valence, trial type, hemisphere, and region, $F(12,288)=6.22, p<.05$. To better explain the five-way interaction we examined amplitudes for different regions (frontal, central, parietal and occipital) separately. A significant interaction effect between group, valence, trial type, and hemisphere emerged only at the occipital site, $F(4,96)=4.96, p=.001$.

A three-way ANOVA was conducted on the amplitudes of the different hemispheres (left and right) separately. An interaction effect between group, valence, and trial type was found only at the P4 electrode, $F(4,96)=5.00, p=.001$. A further 3×3 mixed ANOVA analysis was conducted for happy and sad faces

separately. There was a significant interaction effect between group and trial type for sad faces, $F(4,96)=5.41$, $p < .001$, as well as happy faces, $F(4,96)=5.59$, $p < .001$. A univariate ANOVA revealed that MDD participants had a larger amplitude for sad faces in the positive priming condition compared with the other two groups, $F(2,48)=5.39$, $p=.008$. Moreover, there were marginally significant differences on the amplitude for sad faces in the negative priming condition, $F(2,48)=8.26$, $p < .05$. That is, the amplitude of NC participants was larger compared with the other two groups. MDD participants had a smaller amplitude for happy faces in the control condition compared with the other two groups, $F(2,48)=10.79$, $p < .05$.

A 2×3 repeated-measures ANOVA analysis was conducted for the NC, RMD, and MDD participants separately. There was an interaction effect between valence and trial type in RMD participants, $F(2,32)=15.70$, $p < .001$. Further analysis revealed that RMD participants had a larger amplitude for sad faces compared with happy faces in the positive priming condition, $F(1,32)=7.25$, $p=.011$. Moreover, RMD participants had a smaller amplitude in negative priming condition for happy faces, $F(2,48)=6.49$, $p=.003$, as well as for sad faces, $F(2,48)=18.44$, $p < .001$, compared with other conditions. There was an interaction effect between valence and trial type in MDD participants, $F(2,32)=3.85$, $p=.032$. Exploration of this interaction showed that MDD participants had a larger amplitude for sad faces compared with happy faces at the positive priming condition, $F(1,32)=14.71$, $p=.001$. Furthermore, they had a larger amplitude for happy faces was larger compared with sad faces in the negative priming condition, $F(1,32)=3.45$, $p=.073$. MDD participants also had a smaller amplitude for sad faces in negative priming compared with other conditions, $F(2,48)=9.37$, $p < .001$. None of the other group comparisons were significantly different.

3.3 Discussion

Experiment 2 showed that the MDD participants had larger P1 (O2 electrode) and P3 amplitude (P4 electrode) for sad faces in the positive priming condition compared with the other groups, while they had

marginally significant smaller P3 amplitude for sad faces in the negative priming condition. However, although the effect was marginally significant, the smaller P3 amplitude for sad faces suggested that negative faces were associated with reduced recruitment of attentional resources. In combination with the behavioral data showing reduced inhibition of negative faces, this pattern of results suggests that the MDD participants had deficient distracter inhibition and excessive facilitation of sad faces.

Interestingly, RMD participants had a larger N1 amplitude (O2 electrode) for happy faces and a larger P1 and P3 amplitude for sad faces in the positive priming condition relative to the other conditions, while they had smaller P3 amplitude for both happy and sad faces in negative priming condition. Related to the behavioral data this suggests that the RMD participants had a deficient distracter inhibition and excessive facilitation for both happy as well as sad information.

4 General discussions

The main aim of the present study was to examine cognitive inhibitory and facilitation for emotional information in depressed and remitted depressed individuals in comparison to healthy controls. In Experiment 1, a behavioral paradigm was used that allows examining negative and positive priming. In Experiment 2 we examined neural activity during negative and positive priming in a depressed, remitted depressed, and control sample using ERP. With regard to the behavioral data we observed across the two experiments that depression was associated with impaired inhibition of sad faces. This impaired inhibition of negative information was accompanied by reduced P3 amplitude on these trials. For positive priming in the MDD individuals it was observed that there was an enhanced priming for sad but not for happy faces. In RMD individuals it was observed that there was an excessive facilitation for happy as well as sad faces. This enhanced priming for sad faces was accompanied by enhanced N1 and P1 amplitude on these trials.

The finding that there is deficient inhibition of negative information in MDD is in line with previous

studies using the negative affective priming paradigm (Goeleven et al., 2006; Joormann and Gotlib, 2007). However, the present study improves over these studies as the present paradigm allowed examining facilitation as well as inhibition. In previous studies it was not possible to distinguish between the influence of enhanced facilitation by the distracter or reduced inhibition of the distracting stimulus. Interestingly, the data in the RMD group clearly indicate that inhibitory problems as measured by the NAP task are not necessarily related to enhanced facilitation. In the MDD group enhanced positive priming and reduced negative priming was observed for sad faces.

A second improvement over previous work is the ERP measurement during negative and positive priming of emotional information. In the present study, MDD participants had larger P1 and P3 amplitude for sad faces in the positive priming condition compared with the other groups, while they had smaller P3 amplitude for sad faces in the negative priming condition, which suggested that the MDD participants had deficient distracter inhibition and excessive facilitation of negative stimuli. Furthermore, enhanced and reduced N1, P1, and P3 amplitude of depression in different conditions was observed mainly at the parietal (P4) and occipital (O2) electrodes, which is largely consistent with previous ERP studies on cognitive inhibition in healthy populations (Kathmann et al., 2006; Zhu et al., 2010; Thomas et al., 2007; Ceballos et al., 2003). In a recent first study combining the NAP task with ERP in MDD, it was also found that MDD participants had reduced central-parietal P2 amplitude for negative experimental trials, which is suggestive of cognitive disinhibition (Yao et al., 2010). Although the finding of reduced P3 for negative faces in negative priming condition can be related to previous work on reduced prefrontal control in depression (Canli et al., 2004), the use of ERP methodology does not allow us to give the exact localisation of the source of neural activation. However, functional neuroimaging and EEG studies point to abnormal anterior cingulate activity in depressed subjects during cognitive effort (George et al., 1997; Diener et al., 2009; Diener et al., 2010). Therefore, future studies

need to examine this topic by Low Resolution Electromagnetic Tomography (LORETA) source localisation (Pascual-Marqui, 1997) or by other neuroimaging methods.

In the present study, RMD individuals were also examined to explore whether attentional bias of emotional stimuli is a stable cognitive vulnerability factor perhaps associated with the recurrence of depression. We observed that RMD participants had a deficient distracter inhibition for both happy as well as sad faces which is in line with several other studies (Goeleven et al., 2006; Joormann, 2004; Joormann and Gotlib, 2007). There are several possible explanations for this observation in the RMD participants. It could be that deficient inhibition in depression remains unchanged during remission, with treatment/remission being associated with enhancing processing of positive information. Alternatively, the occurrence of depressive episodes has recently been associated with overall impairments in attentional control, potentially causing reduced cognitive control over emotion processing.

There are several limitations of our study: the sample sizes were relatively small, which limited the interpretation of the results. Furthermore, it is unclear as to whether the results were influenced by antidepressant therapy taken by some of the patients (Leung et al., 2009). However, most of our results remained intact when excluding individuals who took antidepressant medication. Still this does not provide an explanation for the individual differences obtained with depression.

5 Conclusions

In conclusion, this study shows that MDD and RMD participants are characterized by impaired inhibition for affective information. This impairment has a high explanatory value for information-processing bias and the neuropsychological impairments observed in depression. Specification of the cognitive and neuropsychological architecture and experimental research into the functional role of these deficits are the logical next issues on the research agenda.

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